REMARKS

Claims 1-13, 18-19, and 24-25 are pending in the Application. Claims 14-17, and 20-23 are cancelled. Claim 7 has been amended to correct a minor typographical error. Applicants respectfully submit that no new matter has been added.

The Office Action indicates that the prior rejection under 35 U.S.C. §102(a) has been overcome. Applicants gratefully acknowledge withdrawal of the rejection. However, the Office Action indicates that the pending claims are newly rejected under 35 U.S.C. §103. In view of the remarks presented herein, Applicants request reconsideration on the merits, withdrawal of the rejection, and allowance of the claims.

Examiner Interview

Applicants' undersigned representative met with the Examiner on March 10, 2008. Also present at the interview were the Examiner's Supervisor, Shaojia A. Jiang, Applicants' representative Dr. Angeline Babel, and inventor Dr. Paul B. Savage. As noted in the Interview Summary mailed March 18, 2008, Applicants' representatives and the examiners discussed the prior art rejection of record. Applicants appreciate the time and courtesy extended by the examiners during the interview.

Submission of a Declaration was also discussed, as reflected in the Examiner's Interview Summary mailed March 18, 2008. However, upon further consideration, Applicants believe that submission of a Declaration is not necessary at this time in view of the following remarks.

Rejection under 35 U.S.C. §103

In the Office Action of January 9, 2008 ("the Office Action"), claims 1-13, 18-19, and 24-25 were newly rejected under 35 U.S.C. §103(a) as being obvious over Tsuji et al. in view of Defrees et al., Sinay et al., and Kawano et al. The rejection is respectfully traversed.

The Office Action states that Tsuji et al. teaches compounds having the structural features instantly claimed, with the only difference being that the compounds of Tsuji et al. are C-sugars, whereas the claimed compounds are O-sugars. (Office Action at 4). The Office Action further states that Kawano et al. teach that fatty acyl chains in combination with a galactosyl moiety are important for selective activation of NKT cells. (Office Action at 4). The Office Action also

indicates that Sinay et al. and Defrees et al. teach steps needed for the conversion of prior art analogous compounds into the claimed compounds. (Office Action at 4-5).

In order to establish a *prima facie* case of obviousness, it remains necessary for the Patent Office to establish some reason to arrive at the claimed compounds based on the prior art or general knowledge of those of skill in the art. While the Supreme Court in *KSR* rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test in an obviousness inquiry, the Court acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 at 1731 (2007). Since *KSR*, the Federal Circuit has applied the obviousness test to chemical compounds, and has held that "in cases involving new chemical compounds, it remains necessary to identify some reason that would lead a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." *Takeda Chemical Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007). The Board of Patent Appeals and Interferences also recognizes that examiners must identify a reason to make a claimed invention, even in the presence of related art, lest the examiners fall prey to the "unwitting application of hindsight." *Ex parte Joseph K. So*, B.P.A.I. 2007-3967, at 5.

The Office Action alleges that those of skill in the art would be motivated to make the presently claimed compounds because "closely analogous compound[s] have been shown to be good stimulators of NKT cells..." (Office Action at 5). The Office Action further alleges that "Obviousness based on similarity of structure and function entails motivation to make the claimed compound in expectation that compounds similar in structure will have similar properties." However, even in view of the cited references, there would be absolutely no motivation for the person of skill in the art to prepare the presently claimed compounds because: 1) there is an express teaching away in Tsuji et al.; and 2) there would be no expectation of similar properties for structurally similar compounds due to the unpredictablility in the art as demonstrated, for example, by Kawano.

Tsuji et al. teaches away from the claimed compounds.

To derive the claimed compounds from those taught in Tsuji et al., a person of skill in the art would be required to modify the Tsuji et al. compounds by replacing the C-linkage at the

glycosidic bond with an O-linkage. However, this particular modification is expressly disparaged by Tsuji et al. With respect to the O-linked compound "α-GalCer," Tsuji et al. teach:

> [M]ost mammals, including humans, have abundant amounts of α-galactosidase, an enzyme which digests α-GalCer by catalyzing the degradation of α-D-galactoside bonds. As a result, α-GalCer has a short-half life, and therefore its *in vivo* therapeutic effect may be reduced." (Col. 5, lines 40-45).

In addition, Tsuji et al. teach that the C-linked compounds have "improved stability" and "improved therapeutic efficacy" over α–GalCer (Col. 5, lines 50-53) and indicate that C-linked glycolipds are 100 to 1000 times more potent than the corresponding O-linked analogs (Col. 10, lines 5-17). Given the teaching of Tsuji, one of skill in the art seeking to develop compounds for use in this field would not be motivated to use an O-linked glycolipid as a starting compound for further development. Thus, Tsuji et al. teaches away from the use of an O-linkage in developing synthetic compounds in the field of the invention. *See Eli Lilly and Company v. Zenith Goldline Pharms., Inc.*, 471 F.3d 1369, (Fed. Cir. 2006) (holding claimed compound non-obvious despite description of close structural analog in prior art reference because that reference also expressed a strong preference for using a different substituent at another position).

Moreover, the disclosure of O-linked glycolipids in Tsuji can not properly be considered a disclosure of "a non-preferred embodiment." To the contrary, the O-linked compounds are not within the scope of the claims or described as the invention. In fact, the only description of O-linked compounds is a passage seeking to distinguish them from the invention by way of detailing the inferior properties of the O-linked compounds. (Col. 5, lines 40-45). Thus, the O-linked compounds mentioned in Tsuji are not an "embodiment" at all, much less a "non-preferred embodiment."

Further, one of skill in the art would not combine Tsuji et al. with the Kawano et al. reference cited in the Office Action. Kawano et al. discuss various properties of the same O-linked compounds, and modifications of these compounds (all of which have an O-linkage), that Tsuji et al. disparages. Thus, there is simply no teaching in either reference that the compounds should be modified or combined in any particular manner to arrive at the compounds claimed by applicants. *See Alza Corp. v. Mylan Labs., Inc.*, 391 F.3d 1365, 1373 (Fed. Cir. 2004) (holding method of using fentanyl base transdermally was non-obvious because reference that taught

away from the transdermal use of fentanyl would not be combined by one of skill in the art with reference describing fentanyl base.)

Given that the Tsuji and Kawano references provide no motivation to make the claimed compounds, the synthetic methods disclosed in Defrees et al. and Sinay et al. are not relevant to whether the compounds are obvious. That is, when the prior art provides no motivation to make the claimed compounds, references which teach the formation of similar compounds cannot, alone, render the claimed compounds obvious. See *In re Stemniski*, 444 F.2d 581, 586 (C.C.P.A. 1971), affirmed in *In re Dillon*, 919 F.2d 688, 692-93 (Fed. Cir. 1990).

Kawano et al. demonstrates unpredictability in the art.

Even if there were motivation to develop the compounds claimed, one skilled in art of making and testing compounds in the same class as that of the claimed invention is aware that slight structural changes can have a dramatic effect on *in vitro* binding and *in vivo* efficacy. This principle is clearly illustrated, for example, by Kawano et al., which was cited in the Office Action. Kawano et al. teach that *only certain glycolipids* stimulate proliferation of $V_{\alpha}14$ NKT cells, a class of cells suspected to play an important role in IL-12-mediated rejection of tumors. (*See* Kawano et al. at 1628.) While Kawano et al. suspected that glycolipids were important because of the association of CD1 molecules, Kawano et al. noted a wide variety of $V_{\alpha}14$ NKT cell responses due only to small changes in the structure of the glycolipids. (*See* Kawano et al. at 1627.) For example α-GalCer (found in marine sponges) showed the greatest proliferative response, but α-ManCer, differing only in the configuration of the 2-hydroxyl bond, showed no stimulatory activity. (Kawano et al. at 1627.) On the other hand, α-GlyCer, differing from α-GalCer only in the configuration of the 4-hydroxyl bond, showed identical stimulatory activity. (Kawano et al. at 1627.) Thus, Kawano et al. teaches that activity cannot be predicted from structure.

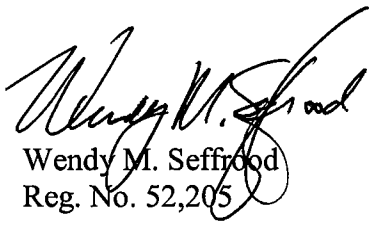
Because one of skill in the art cannot predict whether or not a given glycolipid will stimulate NKT activity, there cannot be a reasonable expectation of success based upon the prior art alone. "[T]o have a reasonable expectation of success, one must be motivated to do more than merely to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful."

Medichem v. Rolabo, 437 F.3d 1157, 1165 (Fed. Cir. 2006) *affirmed in Pfizer v. Apotex*, 480 F.3d 1348 (Fed. Cir. 2007).

CONCLUSION

In view of the remarks presented herein, it is believed that this application is now in condition for allowance. No fee is believed due in connection with this submission. However, if a fee is owed, please charge Deposit Account No. 50-0842.

Respectfully Submitted,



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